REMARKS

The Office Action of August 9, 2005 has been received and reviewed. Claims 8-11 and 22-24 are currently pending in the application. Claims 8-11 and 22-24 stand rejected. Claims 9-11 are amended herein. No new matter has been added. Reconsideration of the application as amended herein is respectfully requested.

Objection to the specification

Applicants have followed the Examiner's suggestions by amending paragraph [0001], line 2, of the specification to read "now U.S. patent No. 6,812,203." Applicants respectfully request removal of the objection.

Claim Rejections—35 U.S.C. § 112, second paragraph

Claims 9-11 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite because it is supposedly not apparent as to whether or not "homology" refers to a similarity (but not sequence identity) of a protein which is functionally and/or structurally equivalent.

While applicants do not agree with the alleged indefiniteness, claims 9-11 have been amended to remove any grounds for objection. Applicants respectfully request removal of the rejection and reconsideration of the claims.

Claim Rejections—35 U.S.C. § 112, first paragraph

Claims 8-11 and 20-24 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly fails to enable one of skill in the art to make and use the claimed invention. Claims 20 and 21 were previously cancelled making the rejection moot as to these claims. Applicants traverse this rejection for the following reasons.

To satisfy the enablement requirement, a specification must teach those skilled in the art how to make and use the scope of the claimed invention without undue experimentation. *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). Furthermore, simulated or prophetic examples are permitted in patent applications (M.P.E.P., § 608.01(p)(II)) and the use of prophetic examples may make a patent enabling. *Atlas Powder Co. v. E.I. DuPont*

di Nemours & Co., 750 F.2d 1569, 1577 (Fed. Cir. 1984).

When determining undue experimentation, the PTO and the courts look to the factors outlined in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The factors include 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

In *In re Wands*, the United States Court of Appeals, Federal Circuit (CAFC) reversed a rejection for lack of enablement for an application claiming monoclonal hybridomas which secrete specific antibodies. *Id.* at 740. The CAFC found the disclosure of the Wands patent enabling because there was a high level of skill in the monoclonal antibody art and, despite the relative unpredictable nature of the technology, the patent disclosure provided guidance and real working examples of the invention. *Id.* at 738.

The CAFC recognized the complexity of the inventive technology but disagreed with the PTO, reasoning that the existing working examples, along with the specification, would allow one of ordinary skill in the art to make and use the invention. *Id.* at 740. The CAFC stated that a considerable amount of experimentation is permissible if it is reasonable with regards to the nature of the art or if the specification provides a reasonable amount of guidance. *Id.* at 737. The CAFC reasoned that the specification contained considerable direction and guidance on how to practice the claimed invention, presented working examples, that all the methods needed to practice the invention were well known and that there was a high level of skill in the art at the time the application was filed. *Id.*

Following the analysis from *In re Wands*, the specification of the instant invention also allows one of skill in the art to make and use the claimed invention without undue experimentation. The specification discloses detailed laboratory protocols and guidance for the full scope of the claims, the referenced methods are well known by those of skill in the art and the specification includes working examples of the claimed invention.

Independent claim 8 recites, in part, an isolated nucleic acid sequence encoding a protein, said protein characterized by an ability to form a complex with receptors of the Tumor Necrosis Factor ("TNF") superfamily including the cytoplasmic domain of CD40 as determined by a yeast

two-hybrid interaction assay or a co-immunoprecipitation assay. Example 1, paragraphs [0077] through [0080] in the specification, provide detailed laboratory methods for isolating proteins that complex with CD40 and for determining the nucleic acid sequence of the isolated proteins. Following the methods in the specification, two novel CD40-complexing proteins were identified and named TTRAP (SEQ ID NO: 1) and 4C4 (SEQ ID NO: 5). In Example 3, the 4C4 protein and TTRAP protein fragments were analyzed and tested for their association with CD40, CD30 and other TNF-receptor proteins. (*See*, Table 1 and FIG. 1). The results show that both TTRAP and 4C4 bind to many different receptors of the TNF-receptor superfamily. *Id.*

Furthermore, Example 5 in the specification provides detailed instructions for performing a co-immunoprecipitation assay for isolating those proteins characterized by an ability to form a complex with TNF-receptor proteins. Western blot analysis of the immunoprecipitated fractions showed that TTRAP complexes with the TNF-receptor proteins TNF-RII and TRAF5. (Specification, paragraphs [0096] and [00101]).

Additionally, Example 9 provides a list of isolated nucleic acid sequences encoding a protein with the ability to complex with TNF receptors. The list includes the Bloom syndrome, the human nuclear autoantigen and the human homologue of the mouse BP75 protein .

On page 4 of the Office Action, the Examiner states that it requires a great deal of effort and tests to practice the scope of the claimed invention. However, in light of the detailed instructions and working examples in the specification, applicants submit that one of skill in the art could make and use the claimed invention with reasonable efforts. The CAFC in *In re Wands* was not concerned so much about the amount of experimentation necessary, only that it was unreasonable for those of skill in the art. *In re Wands*, 858 F.2d at 737 The CAFC stated that a considerable amount of experimentation is permissible if it is reasonable with regards to the nature of the art or if the specification provides a reasonable amount of guidance. *Id.*

In regards to the Examiner's concerns that mutations in TRAF4 result in elimination of the signaling capability of the TNF-receptor, applicants submit that the working examples in the specification show that the disclosed methods work and accomplish the goal of the claimed invention. Moreover, independent claim 8 recites a nucleic acid encoding a protein with an ability to form a complex with TNF-receptors that is determined by a yeast two-hybrid or co-immunoprecipitation assay. The claim does not recite the signaling capability or biological

function of the TNF-receptor protein.

On page 5 of the Office Action, the examiner states that the disclosure fails to teach a common attribute and characteristics that identify the peptide. However, applicants assert that independent claim 8 recites, in part, that the identifying characteristics are a protein that complexes with TNF-receptor as determined by the recited assays and comprises amino acids 54-140 of SEQ ID NO:2 or a fragment of amino acids 54-140 of SEQ ID NO: 2 at least 10 consecutive amino acids in length. As such, the disclosure provides multiple identifying characteristics of the peptide.

Finally, the Examiner expresses concern, despite the high skill in the art, that the specification requires undue experimentation by those of skill in the art. (Office Action, page 6). The Examiner also characterizes the scope of the claims as "[s]orting out core domain(s) critical for the peptide fragment that comprises 10 or more than 10 amino acid residues of SEQ ID NO: 2." Applicants respectfully submit that the scope of the claim is incorrectly characterized. Independent claim 8 does not include elements of sorting out core domains critical for the peptide fragment. Claim 8 recites an isolated nucleic acid sequence encoding a protein, said protein characterized by an ability to form a complex with receptors of the Tumor Necrosis Factor superfamily including the cytoplasmic domain of CD40 as determined by a yeast two-hybrid interaction assay or a co-immunoprecipitation assay. As such, one of skill in the art would not require undue experimentation involving any sorting of core domains to make and use the claimed invention.

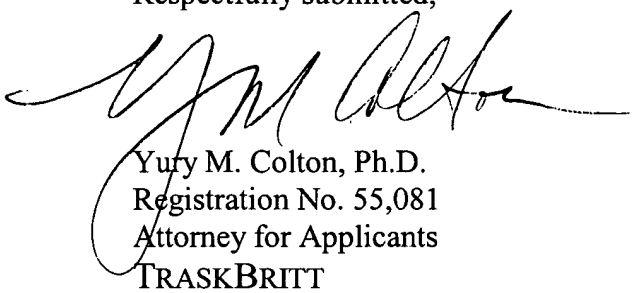
Therefore, the specification is enabling for the scope of the instant claims because, like in *In re Wands*, the biological methods and techniques are predictable and well known in the art, the specification provides significant and detailed guidance and includes real working examples applicable to the entire scope of the claimed invention.

Accordingly, applicants respectfully request removal of the rejection and kindly ask reconsideration of the claims.

CONCLUSION

In view of the foregoing amendments and remarks, the applicants submit that the claims define patentable subject matter and a notice of allowance is requested. Should questions exist after consideration of the foregoing, the Office is kindly requested to contact the applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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